

REMARKS

In response to the Office Action mailed November 2, 2006, Applicants have amended claims 1 and 3 and canceled claims 4, 6-8, 10 and 18-24. Support for all the above amendments may be found throughout the specification as originally filed, for example at page 47, lines 11-15 and page 48, lines 10-12. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 1-3 and 11-12 are pending in the application. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Title of the Invention

The PTO alleges that the title of the invention is not descriptive and requires a new title. Without acquiescing to this assertion, Applicants hereby amend the title to METHODS FOR ELIMINATING UNDESIRE SUBPOPULATIONS OF T CELLS.

Priority

It appears that the PTO has not granted Applicants the benefit of the filing date of earlier filed applications because specific reference thereto does not appear as the first sentence of the specification following the title.

Applicants respectfully traverse the PTO's determination of priority and submit that the PTO asserts in paragraph 4 of the Action:

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121, or 365(e), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the

specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. (Emphasis added.)

Applicants submit that information appearing in an Application Data Sheet (ADS) is considered part of the application. According to the MPEP § 601.05:

Since the application data sheet, if provided, is considered part of the application, the specific reference to an earlier filed provisional or nonprovisional application in the application data sheet satisfies the "specific reference" requirement of 35 U.S.C.119(e)(1) or 120, and it also complies with 37 CFR 1.78(a)(2) (iii) or (a)(5)(iii). Thus, a specific reference does not otherwise have to be made in the specification, such as in the first sentence(s) of the specification. (Emphasis added.)

Accordingly Applicants submit that they are entitled to the benefit of the earlier filing date of June 28, 2002 as listed on pages 4 and 5 of the ADS filed with the instant application. Reconsideration is respectfully requested.

Trademarks

The PTO notes the use of trademarks in the application.

Applicants have amended the specification to indicate with all capital letters and/or with the trademark symbol certain trademarks that were not clearly indicated. Applicants note that every effort has been made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections – 35 U.S.C. § 112, second paragraph (indefiniteness)

Claims 1-4, 6-8, 10-12 and 18-24 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. In particular, the PTO asserts that the metes and bounds of "a substantial portion" are ambiguous and unclear because the specification provides no teaching or definition of what Applicants considered to be "a substantial portion." The PTO further asserts that claim 7 is indefinite because no SEQ ID NOs are provided for the recited proteins. The PTO alleges that since different laboratories may have the same name for different

proteins, the claims are ambiguous. Dependent claims 20-24 stand rejected as lacking antecedent basis since claim 3 does not recite “the first or the second agent.”

Applicants respectfully traverse the rejection and submit that the specification as filed clearly defines what is considered a “substantial portion,” for example at page 26, lines 22-25. As such, Applicants submit that the skilled artisan would readily understand the metes and bounds of the claims.

Concerning claim 7, Applicants respectfully disagree and submit that the skilled artisan would readily appreciate the appropriate sequence for the recited autoantigens, and would be able to readily access such information in any of a variety of publicly available sequence databases. However, without acquiescing to the rejection and solely to advance prosecution Applicants have canceled claim 7. This amendment is made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Claims 20-24 have been canceled without prejudice or acquiescence, thereby obviating the rejection of these claims.

In view of the amendments and above remarks, reconsideration of the claims and withdrawal of the rejection are respectfully requested.

Claim Rejections – 35 U.S.C. § 112, first paragraph (enablement)

Claims 1-4, 6-8, 10-12 and 18-24 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. In particular, the PTO asserts that the specification, while being enabling for a method for eliminating a substantial portion of clonal T cells from a mixed population of cells comprising exposing the mixed population of T cells to a surface wherein the surface has attached thereto anti-CD3 and anti-CD28 antibodies, does not reasonably provide enablement for such methods comprising exposing a population of T cells to any pro-apoptotic composition as recited in claims 1-4 or the autoantigens recited in claims 6-8 or the agents recited in claim 18.

Without acquiescing to the rejection and solely to advance prosecution, Applicants have amended the claims to recite “A method for eliminating at least a substantial

portion of a clonal T cell subpopulation from a mixed population of T cells from an individual, comprising, exposing a population of cells, wherein at least a portion thereof comprises T cells, to a surface, wherein the surface has attached thereto an anti-CD3 antibody and an anti-CD28 antibody, or antigen-binding fragments thereof, wherein the ratio of surface to cells is at least 5:1...” Applicants reserve the right to prosecute any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Applicants submit that, as noted in the Action at paragraph 11, the presently claimed invention is enabled by the specification. Reconsideration of the claims and withdrawal of the rejection are respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 1 and 18 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by WO 94/28926. In particular, the PTO asserts that the reference teaches elimination of a subpopulation of T cells by exposing the cells to anti-CD3 antibody in conjunction with IL-2 or IL-4.

Claim 18 has been canceled without prejudice or acquiescence. Applicants respectfully traverse this rejection as it may apply to claim 1 as amended. Applicants submit that the ‘926 reference teaches only the elimination of certain T cell populations by exposure to IL-2 followed by antigen or other stimulation. Nowhere does this reference teach the claimed method of eliminating at least a substantial portion of a clonal T cell subpopulation from a mixed population of T cells from an individual, comprising, exposing T cells to a surface, wherein the surface has attached thereto an anti-CD3 antibody and an anti-CD28 antibody, or antigen-binding fragments thereof, wherein the ratio of surface to cells is at least 5:1. As such, this reference does not anticipate the presently claimed invention. Reconsideration of the claims and withdrawal of the rejection are respectfully requested.

Claim Rejections – 35 U.S.C. § 102

Claims 1-4, 11, 12 and 18-24 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by U.S. Patent 6,352,694 or WO 03/067221 or WO 03/024989.

Applicants respectfully traverse the rejection on the following grounds. As an initial matter, Applicants note that WO 03/067221 and WO 03/024989 are not prior art under § 102(b) in view of Applicants' earliest priority date of June 28, 2002 as discussed above with regard to Applicants' priority claim. Specifically, WO 03/067221 was published on August 14, 2003 and WO 03/024989 was published March 27, 2003, both after the earliest priority date of the instant application. Applicants address the rejection regarding the '694 patent as it may apply to amended claims 1-3 and 11-12. Claims 4 and 18-24 have been canceled without acquiescence or prejudice. The amendments to the claims were made without acquiescing to the rejection and solely to advance prosecution. Further Applicants reserve the right to prosecute any subject matter removed or modified by the amendment in a related application.

Applicants traverse the rejection and submit that nowhere does the '694 patent teach the presently claimed method. The PTO asserts that the '694 patent teaches a method of expanding T cells using anti-CD3 and anti-CD28 antibodies attached to beads wherein the ratio of beads to cells is high, *e.g.*, 10:1. Applicants submit that the '694 patent does not teach using beads to cells at any ratio higher than 3:1. Throughout the examples, a 3:1 ratio of surface to cells is used. The 10:1 ratio cited by the PTO refers, in fact, to the ratio of cells to surface, the surface in this case being cells expressing B7-1, which can be used to costimulate T cells. In particular, the patent states at column 9, lines 33-39 "The ratio of T cells to B7-expressing cells can be anywhere between 10:1 to 1:1, preferably 2.5:1 T cells to B7-expressing cell." This ratio is exactly the opposite of what is presently being claimed (*i.e.*, surface to cells). Thus, the '694 patent does not anticipate the presently claimed method of eliminating at least a substantial portion of a clonal T cell subpopulation comprising, exposing T cells to a surface having attached thereto an anti-CD3 antibody and an anti-CD28 antibody, or antigen-binding fragments thereof, wherein the ratio of surface to cells is at least 5:1. Reconsideration of the claims and withdrawal of the rejection are respectfully requested.

Claim Rejections – 35 U.S.C. § 103

Claims 1 and 6-8 stand rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over WO 94/28926 in view of the known fact disclosed in the specification at pages 27-28.

Without acquiescing to the rejection and solely to advance prosecution, claim 1 has been amended to specifically recite the use of a surface having attached thereto anti-CD3 and anti-CD28 antibodies. Further, claims 6-8 have been canceled without prejudice. As such, Applicants submit that the rejection has been obviated. In particular, Applicants submit, as noted above, that the '926 reference teaches only the elimination of certain T cell populations by exposure to IL-2 followed by antigen or other stimulation. Nowhere does this reference teach or even suggest the claimed method of eliminating at least a substantial portion of a clonal T cell subpopulation from a mixed population of T cells from an individual, comprising, exposing T cells to a surface, wherein the surface has attached thereto an anti-CD3 antibody and an anti-CD28 antibody, or antigen-binding fragments thereof, wherein the ratio of surface to cells is at least 5:1. Withdrawal of the rejection is respectfully requested.

Provisional Rejection under Obviousness-type Double Patenting

Claims 1-4, 6-8, 10-12 and 18-24 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of co-pending Application Nos. 20060121005, 20050226857, 20050214942, 20050153447, 20050084967, 20040241162, 20040151704, 20040005298, 20030235908, 20030124122, 20030119185, 20030082806, 20030022210, 20020119568, and 20020058019.

Applicants respectfully request that the rejection over the claims in Application No. 20060121005 be held in abeyance until the claims in the instant application are determined to be allowable. Applicants will consider filing a preliminary amendment in Application No. 20060121005 or a terminal disclaimer at that time.

Applicants respectfully traverse the rejection over the remaining applications on the following grounds. Application Nos. 20040151704, 20040005298, 20030082806 and 20030022210 are abandoned. Further, a preliminary amendment was filed on January 16, 2007

in response to the Restriction Requirement issued by the PTO in related Application No. 20050084967, a CIP of the present application, canceling claims 1-4 and 6-73. Accordingly, claims directed to methods of eliminating subpopulations of T cells are no longer pending in that application.

The claims in Application Nos. 20050226857, 20050214942, 20050153447, 20040241162, 20030235908, 20030124122, 20030119185, 20020119568, 20020058019 do not teach or suggest the use of a high bead to cell ratio for eliminating at least a substantial portion of a clonal T cell subpopulation. In particular, the claims in these applications are generally directed to methods of expanding polyclonal or antigen-specific T cells, an apparatus and methods of aggregating T cells using the apparatus, and do not recite the high ratio of beads to cells necessary for eliminating subpopulations of T cells. As such, the present claims are not obvious in view of the cited references. Reconsideration of the claims and withdrawal of the provisional rejection is requested.

Notwithstanding the above remarks, Applicants will consider filing a terminal disclaimer over the cited co-pending applications once the claims in the instant application are determined to be otherwise allowable.

In view of the above amendments and remarks, the claims are now believed to be in condition for allowance. A good faith effort has been made to place the application in condition for allowance. However, should any further issue require attention prior to allowance, the Examiner is requested to contact the undersigned at 206-622-4900 to resolve same.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,
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